#### INTERNATIONAL SEARCH REPORT

Inte nal Application No PCT/I L2004/000921

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07K16/40 A61K39/395 A61P37/00 According to International Patent Classification (IPC) or to both national classification and IPC **B. FIELDS SEARCHED** Minimum documentation searched (classification system followed by classification symbols) IPC 7 C07K A61K C12N Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) EPO-Internal, Sequence Search C. DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate, of the relevant passages Category ° Relevant to claim No. 1,3, 7-13, US 5 854 003 A (ROTHE MIKE ET AL) Χ 29 December 1998 (1998-12-29) 17-20, 30, 36-40. 45-48. 53-57, 62-65, 70,75-85 column 4, line 5 - line 19; table 2
column 2, line 58 - line 67 -/--Further documents are listed in the continuation of box C. Patent family members are listed in annex. Special categories of cited documents: later document published after the international filing date or priority date and not in conflict with the application but "A" document defining the general state of the art which is not considered to be of particular relevance cited to understand the principle or theory underlying the invention "E" earlier document but published on or after the International "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such docu-"O" document referring to an oral disclosure, use, exhibition or ments, such combination being obvious to a person skilled in the art. other means document published prior to the international filing date but later than the priority date claimed "&" document member of the same patent family Date of the actual completion of the international search Date of mailing of the international search report 3 0. 06. 2005 27 April 2005 Name and mailing address of the ISA Authorized officer European Patent Office, P.B. 5818 Patentiaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016 van Klompenburg, W

## **INTERNATIONAL SEARCH REPORT**

Inte al Application No
PCT/IL2004/000921

Atton) DOCUMENTS CONSIDERED TO BE RELEVANT  Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Citation of document, with indication, where appropriate, of the relevant passages	neievant to cialm No.
	<u></u>
WO 97/37016 A (BOLDIN MARK ; METT IGOR (IL); WALLACH DAVID (IL); MALININ NIKOLAI (IL)) 9 October 1997 (1997-10-09) cited in the application	1,3, 7-13, 17-20, 30, 36-40, 45-48, 53-57, 62-65, 70,75-85
claims 22,26; figure 6; examples 1-6	
WO 95/26365 A (UNITED BIOMEDICAL, INC; WANG, CHANG, YI) 5 October 1995 (1995-10-05)	1,2,5,7, 8,30,31, 33, 35-37, 60,65, 66,68,84
SEQ ID NO: 38, claims 1-44 abstract	
US 5 030 565 A (NIMAN ET AL) 9 July 1991 (1991-07-09)	1,2,4,7, 8,30-32, 35-37, 59, 65-67,84
claim 2	
WO 90/10231 A (REPLICO MEDICAL AB) 7 September 1990 (1990-09-07)	1,2,6,8, 30,31, 34-37, 61,65, 66,69,84
claim 2	
US 2003/082519 A1 (SCHUBART DANIEL ET AL) 1 May 2003 (2003-05-01) paragraphs [0018], [0044], [0047], [0126]; claims 4,8	1-58, 62-85
CHEN DANYING ET AL: "NIK is a component of the EGF/heregulin receptor signaling complexes."  ONCOGENE. 10 JUL 2003, vol. 22, no. 28, 10 July 2003 (2003-07-10), pages 4348-4355, XP002315069 ISSN: 0950-9232 figure 4	1-58, 62-85
	claims 22,26; figure 6; examples 1-6 W0 95/26365 A (UNITED BIOMEDICAL, INC; WANG, CHANG, YI) 5 October 1995 (1995-10-05)  SEQ ID NO: 38, claims 1-44 abstract US 5 030 565 A (NIMAN ET AL) 9 July 1991 (1991-07-09)  claim 2 W0 90/10231 A (REPLICO MEDICAL AB) 7 September 1990 (1990-09-07)  claim 2 US 2003/082519 A1 (SCHUBART DANIEL ET AL) 1 May 2003 (2003-05-01) paragraphs [0018], [0044], [0047], [0126]; claims 4,8  CHEN DANYING ET AL: "NIK is a component of the EGF/heregulin receptor signaling complexes." ONCOGENE. 10 JUL 2003, vol. 22, no. 28, 10 July 2003 (2003-07-10), pages 4348-4355, XP002315069 ISSN: 0950-9232 figure 4

## INTERNATIONAL SEARCH REPORT

Inte I Application No
PCT/I L2004/000921

	(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT							
	ation) DOCUMENTS CONSIDERED TO BE RELEVANT							
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.						
L,P, X	WO 03/087380 A (RAMAKRISHNAN PARAMESWARAN; SHMUSHKOVICH TAISIA (IL); WALLACH DAVID (I) 23 October 2003 (2003-10-23)	1,3, 7-13, 17-20, 30, 36-40, 45-48, 53-57, 62-65,						
	claims 26,32,49; figures 2,3; examples 7,9	62-65, 70,75-85						

International application No. PCT/IL2004/00⊙921

### INTERNATIONAL SEARCH REPORT

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. X Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 70-81 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:
see additional sheet
$\cdot$
1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. X As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4-6,14-16,21-29,32-34,42-44,50-52,59-61,67-69 72-74 (completely) and claims 1-3, 7-13,17-20,30,31,35-41,45-49,53-58 62-66,70,71,75-85 (partially)
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
—Remark-on-Protest  The additional search fees were accompanied by the applicant's protest.  X  No protest accompanied the payment of additional search fees.

#### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1 Claims :1,3,7-13,17-20,30,36-40,45-48,53-57,62-65,70,75-85 (all partially)

A preparation comprising one or more antibodies being capable of binding to SEQ ID NO:1. A method of preparing a monoclonal antibody. An antibody, a monoclonal antibody, a pharmaceutical composition. A method of regulating a biochemical activity of a NIK molecule. A composition of matter comprising a substrate covalently attached to a polypeptide of SEQ ID NO:1. The use of a preparation comprising an antibody recognizing SEQ ID NO:1 in the manufacture of a medicament. A method of treatment. A method for purification of a NIK binding protein. The use of an antibody for an ELISA assay and the usr of an antibody for immune purification of NIK.

Invention 2-6: Claims 1,3,7-13,17-20,30,36-40,45-48,53-57,62-65,70,75-85 (all partially)

As invention 1, but whereby invention 2 is characterized by SEQ ID NO:2, invention 3 by SEQ ID NO:3 etc.

Invention 7 Claims: 4,14-16,21,24,27,32,42,50,59,67,72 completely, 1-3,7-13,17-20,30,31,35-41,45-49,53-58,62-66,70,71, 75-85(partially)

As invention1, but characterized by SEQ ID NO:7 and additionaly hybidoma clone No-I-3092 and monoclonal antibodies generated by it.

Invention 8 Claims:
1-3,7-13,17-20,30,31,35-41,45-49,53-58,62-66,70,71,75-85(partially)

As invention 1, but characterized by SEQ ID: NO 8

Invention 9: claims 1,3,7-13,17-20,30,36-40,45-48,53-57,62-65,70,75-85 (all partially)

As invention 1, but characterized by SEQ ID NO:9

Invention 10 Claims:
1,3,7-13,17-20,30,36-40,45-48,53-57,62-65,70,75-85 (all partially)

### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

As invention 1, but characterized by SEQ ID NO:10

Invention 11 Claims: 5,22,25,28,33,43,51,60,68,73 (completely), 1-3,7-13,17-20,30,31,35-41,45-49,53-58,62-66,70,71,75-85 (partially)

As invention1, but characterized by SEQ ID NO:11 and additionaly hybridoma clone No-I-3093 and monoclonal antibodies generated by it.

Invention 12, Claims: 6,23,26,29,34,44,52,61,69,74 (completely), 1-3,7-13,17-20,30,31,35-41,45-49,53-58,62-66,70,71, 75-85(partially)

As invention 1, but characterized by SEQ ID NO:12 and additionally hybridoma clone No-I-3095 and monoclonal antibodies generated by it.

Invention 13 Claims: 1-3,7-13,17-20,30,31,35-41,45-49,53-58,62-66,70,71, 75-85(partially)

As invention 1, but characterized by SEQ ID NO: 13

Invention 14 Claims: 1-3,7-13,17-20,30,31,35-41,45-49,53-58,62-66,70,71,75-85(partially)

As invention 1, but characterized by SEQ ID NO: 15

Inventions 15-18: Claims 1,3,7-13,17-20,30,36-40,45-48,53-57,62-65,70,75-85 (all partially)

As invention 1, but whereby invention 15 is characterized by SEQ ID NO: 18, invention 16 is characterized by SEQ ID NO: 19, invention 17 by SEQ ID NO: 20 and invention 18 by SEQ ID NO: 22.

# INTERNATIONAL SEARCH REPORT Information on patent family members

Inter.... al Application No PCT/IL2004/000921

					PC1/1L2004/000921	
Patent document cited in search report		Publication date		Patent family member(s)		Publication date
US 5854003	A	29-12-1998	US AU CA EP JP US WO	5843721 724178 8382098 2295999 1012174 2001510348 5844073 9901471	B2 A A1 A1 T A	01-12-1998 14-09-2000 25-01-1999 14-01-1999 28-06-2000 31-07-2001 01-12-1998 14-01-1999
WO 9737016	A	09-10-1997	AU BG CCZ EE HU JP NZ PL SK	1221449 9803183 4309 9800322 0894130 9902429 9737016 2000507826 984551	A A A A A B A A A A A A A A A A A A A A	03-05-2001 22-10-1997 31-05-1999 03-08-1999 09-10-1997 30-06-1999 12-05-1999 26-02-2004 15-04-1999 03-02-1999 28-10-1997 27-06-2000 24-11-1998 28-02-2000 15-03-1999 07-05-1999
WO 9526365	А	05-10-1995	AU CA CN EP JP WO	2195395 2186595 1146772 0811016 9510975 9526365	A1 A A1 T	17-10-1995 05-10-1995 02-04-1997 10-12-1997 04-11-1997 05-10-1995
US 5030565	A	09-07-1991	US US AAU AAA CAE EP IT JP JS OO ZA	5733738 6551789 5972629 113962 633253 3386089 580738 3395084 1219232 3486356 0152477 0592026 1177968 2592581 7284398 61500068 5015571	A A A B1 A T B2 A B2 A1 D1 T2 A1 B B2 A T A1 A1 A1 A1 A1 A1 A1 A1 A1 A1 A1 A1 A1	08-10-1996 07-01-1997 28-07-1998 31-03-1998 22-04-2003 26-10-1999 15-11-1994 28-01-1993 24-08-1989 02-02-1989 12-03-1985 17-03-1987 15-12-1994 01-06-1995 28-08-1985 13-04-1994 03-09-1987 19-03-1997 31-10-1995 16-01-1986 14-05-1991 28-02-1985 27-03-1985

# INTERNATIONAL SEARCH REPORT Information on patent family members

International Application No PCT/IL2004/000921

Patent document cited in search report		Publication date		Patent family member(s)	Publication date
WO 9010231	Α	07-09-1990	AU AU CA DE DE EP JP WO US	640921 B2 5283490 A 2048655 A1 69024951 D1 69024951 T2 0461193 A1 4507286 T 3271666 B2 9010231 A1 6242174 B1	09-09-1993 26-09-1990 03-09-1990 29-02-1996 01-08-1996 18-12-1991 17-12-1992 02-04-2002 07-09-1990 05-06-2001
US 2003082519	A1	01-05-2003	EP	1201765 A2	02-05-2002
WO 03087380	A	23-10-2003	AU CA CA EP EP WO	2003222415 A1 2003226607 A1 2482387 A1 2482718 A1 1499724 A1 1499729 A1 03087374 A1 03087380 A1	27-10-2003 27-10-2003 23-10-2003 23-10-2003 26-01-2005 26-01-2005 23-10-2003 23-10-2003